

CLAIMS

We claim:

1. A conjugate comprising a first sequence and a second sequence, wherein the first sequence comprises a protein which binds to an antigen presenting cell (APC), or a polynucleotide encoding therefor, and wherein the second sequence comprises a protein which modulates a T cell signalling pathway, or a polynucleotide coding therefor.
2. The conjugate according to claim 1, wherein the conjugate is a fusion protein.
3. The conjugate according to claim 1, wherein the second sequence is a protein for T cell receptor signalling transduction, or a polynucleotide coding therefor.
4. The conjugate according to claim 3, wherein the second sequence is a protein for activation of a T cell costimulatory molecule, or a polynucleotide coding therefor.
5. The conjugate according to claim 1, wherein the second sequence is a protein for Notch signalling transduction or a polynucleotide coding therefor.
6. The conjugate according to claim 5, wherein the second sequence is Notch, or a fragment or analogue thereof which retains Notch signalling transduction activity, or a polynucleotide coding therefor.
7. The conjugate according to claim 5, wherein the second sequence is a Notch ligand, or a fragment or analogue thereof which retains Notch ligand signalling transduction activity, or a polynucleotide coding therefor.
8. The conjugate according to claim 7, wherein the second sequence is derived from Delta or Serrate, or a polynucleotide coding therefor.
9. The conjugate according to claim 5, wherein the second sequence is selected from the group consisting of:
 - a) a protein that upregulates expression or activity of Notch, a Notch ligand or a downstream component of Notch signalling pathway;
 - b) an antibody; and
 - c) a polynucleotide encoding a) or b).
10. The conjugate according to claim 9, wherein the second sequence is selected from the group consisting of Noggin, Chordin, Follistatin, Xnr3, fibroblast

growth factors, immunosuppressive cytokines, derivatives, fragments, variants and homologues thereof, and polynucleotides coding therefor.

11. The conjugate according to claim 10, wherein the second sequence is an immunosuppressive cytokine selected from the group consisting of IL-4, IL-10, IL-13, TGF- β , SLIP3 ligand, and a polynucleotide coding therefor.

12. The conjugate according to claim 5, wherein the second sequence is a protein for Notch signalling inhibition, or a polynucleotide coding therefor.

13. The conjugate according to claim 12, wherein the second sequence is selected from the group consisting of:

- 10 a) a protein that downregulates expression or activity of Notch, a Notch ligand or a downstream component of Notch signalling pathway;
- b) an antibody; and
- c) a polynucleotide encoding a) or b).

14. The conjugate according to claim 13, wherein the second sequence is selected from the group consisting of Toll-like receptors (TLRs), cytokines, bone morphogenic proteins (BMPs), BMP receptors, activins, derivatives, fragments, variants and homologues thereof, and polynucleotides coding therefor.

15. The conjugate according to claim 14, wherein the second sequence is a cytokine selected from the group consisting of IL-12, IFN- γ , TFN- α , and a polynucleotide coding therefor.

16. The conjugate according to claim 1, wherein the first sequence is a protein which binds to an APC surface molecule, or a polynucleotide coding therefor.

17. The conjugate according to claim 16, wherein the APC surface molecule is an MHC class II molecule, CD205 (DEC205), CD204 (Scavenger receptor), CD14, CD206 (Mannose receptor), a TLR, Langerin (CD207), DC-SIGN (CD209), Fc γ receptor 1 (CD64), Fc γ receptor 2 (CD32), CD68, CD83, CD33, CD54 or BDCA-2,3,4.

18. The conjugate according to claim 16, wherein the first sequence is a protein which binds to an MHC class II molecule.

19. The conjugate according to claim 1, wherein the first sequence is a superantigen, or is derived therefrom.

20. The conjugate according to claim 19, wherein the superantigen is of bacterial or viral origin.

21. The conjugate according to claim 19, wherein the first sequence comprises the MHC class II binding domain of the superantigen.

22. The conjugate according to claim 19, wherein the superantigen is a Staphylococcal enterotoxin (SE) selected from the group consisting of SEA, SEB,
5 SEC, SED, SEE and SEH.

23. The conjugate according to claim 21, wherein the superantigen is Toxic Shock syndrome toxins (TSST-1).

24. The conjugate according to claim 19, wherein the superantigen is a Streptococcal enterotoxin (SPE) selected from the group consisting of SPEA, SPEC
10 and SSA.

25. A polynucleotide sequence encoding the conjugate of claim 1.

26. An expression vector comprising the polynucleotide sequence of claim
25.

27. A host cell transformed with the expression vector of claim 26.

15 28. A method for preparing a conjugate comprising culturing the host cell of claim 27 under conditions which provide for expression of the conjugate.

29. A conjugate prepared by the method of claim 28.

20 30. A method of targeting a protein for Notch signalling modulation, or a polynucleotide coding therefor, to an APC comprising exposing the APC to the conjugate according to claim 1.

31. A composition comprising the conjugate of claim 1 and a pharmaceutically acceptable excipient, diluent or carrier.

25 32. A method of preventing or treating a disease or infection a subject in need thereof, comprising administering the conjugate according to claim 1 to the subject.

33. The method according to claim 32, wherein the disease is a T-cell mediated disease.